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The EGF receptor system in head and neck carcinomas and normal tissues. Immunohistochemical and quantitative studies.

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The EGF receptor (EGF receptor) and two of the ligands, transforming growth factor alpha (TGF-alpha) and epidermal growth factor (EGF), exert mitogenic activities in epithelial cells. Hence, the overall aim of this work was delineation of the EGF receptor system in head and neck carcinomas, which in the majority of cases are epithelial derived tumours. Chapter 1 is a general introduction to head and neck carcinomas and the relevance of the EGF receptor system in this context. Chapter 2 focuses on the immunohistochemical distribution of TGF-alpha in normal human tissues, while previous studies dealing with the growth factor in head and neck carcinomas revealed other localizations in normal cells. TGF-alpha was detected with monoclonal as well as polyclonal antibodies. The results showed that the growth factor is widely distributed in normal human tissues and thus not limited to malignant cells. Chapter 3 describes the immunohistochemical localization of the EGF receptor in 55 patients with squamous cell carcinoma in the head and neck region. The study included adjacent normal mucosa and in 12 cases additional dysplastic areas were present. The EGF receptor was found in the basal cell layer in normal oral and laryngeal mucosa. In sections from patients who had received preoperative irradiation the receptor was in addition seen on the spinous cells. In dysplastic epithelial all cells stained for the EGF receptor. The majority of the head and neck carcinomas expressed the EGF receptor. In poorly differentiated tumours almost all cells were positive for the receptor. Sections from moderately and well differentiated tumours demonstrated a reduction in the extent of stained areas, paralleling the situation observed in the differentiated upper layers of normal oral and laryngeal mucosa. Furthermore, this chapter describes the EGF receptor quantitatively in 60 patients with head and neck carcinoma. This study was performed in order

to evaluate if overexpression of the EGF receptor was a common motif for head and neck carcinomas. The level in tumour biopsies was compared with the level in the patients' corresponding normal mucosa. An enzyme-linked immunosorbent assay detecting protein epitopes of the receptor was employed. Overexpression of the receptor was found in the majority of cases. The overexpression was further correlated to clinicopathological parameters. However, no significant correlations were found although the mean values increased with increased tumour size and advanced clinical stage. The use of quantitative assays are further discussed and limitations are emphasized with respect to heterogeneity at the EGF receptor level and the varying stromal components in malignant tissues. Despite these problems the relevance of the EGF receptor a therapeutic situation is illustrated with e.g. EGF receptor antibodies and tyrosine-kinase inhibitors. Chapter 4 focuses on the immunohistochemical expression of EGF and TGF-alpha in carcinomas from same 55 patients. This study included adjacent normal mucosa in which the growth factors were expressed above the basal cell layer. The majority of the tumours expressed both growth factors and none of the sections were negative for both EGF and TGF-alpha. In biopsies from moderately and well differentiated tumours the growth factors were demonstrated in the more differentiated cells. However, in poorly differentiated tumours the cells were positive for EGF and TGF-alpha. Chapter 5 describes immunohistochemical and quantitative changes of salivary EGF, amylase and haptocorrin following radiotherapy for oral cancer. This study was initiated because irradiated oral and laryngeal mucosa have demonstrated staining for the receptor in the basal cell layer as well as in the spinous cells, indicating an upregulation of the receptor in response to lack of EGF. In normal biopsies from the glandula submandibularis and glandula parotis, EGF and amylase were demonstrated in the serous acini, whereas haptoc

Publication Types:

- Review
- Review, Academic

PMID: 9587699 [PubMed - indexed for MEDLINE]

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